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(54) Title: USE OF THE TARCHONANTHUS CAMPHORATUS

(57) Abstract

Use of Tarchonanthus camphoratus parts and its derivatives in insect-repelling, anti-irritating, soothing, anti-oedema, decongesting formulations and compositions.

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USE OF THE TARCHONANTHUS CAMPHORATUS

This invention is referred to new uses of the *Tarchonanthus camphoratus*, utilization of its leaves, roots and branches either fresh, dried, soaked, extracted or in the form of essential oil.

5 The *Tarchonanthus camphoratus* is a shrub rearing in the wild in different African regions especially in the Rift uplands area. An experimental growing took also place in Italy (Canzonieri and Spica; Gazz. Chim. Ital. 1882, 227).

10 The shrub, mostly unknown by botanists, has different names such as: Wild cotton, Sage wood, Wilde-salie, Kamferhout, Kamferbos, Sieriehout, Vaalbos, Veld-vaalbos, Vaaibos, Sauto Mofahlana, Rolog e Thaalaping mohathla, well known in the local Swahili dialect with the name of "Leleshua", in the abissianian language "Ebok" and so on, or simply with the botanic name of *Tarchonanthus camphoratus*.

15 The *Tarchonanthus camphoratus* is a shrub reaching 2-4 m height; belonging to the Composite family, it has regular branches with velutinous white-greenish oval or lanceolate shaped leaves ranging from 4 to 13 cm lenght having a strong camphorated aromatic smell, whence its Linneana denomination.

20 This plant, with its wool-like, spike shaped flower heads is mentioned only in "The Medicinal and Poisonous Plants of Southern Africa" by John Mitchell Watt and Maria Gerdina Breyer-Brandwijk - Edinburgh, 1932 and in Paolo Rovesti's communication, presented at the XXIX International Congress of Industrial Chemistry

in Paris in December 1956, "Ecological influences on the composition of the essential oils".

In the literature, mentioned herewith, various applications of this plant are known.

5 - Engler mentions this species as used only for wood by the Usambara in Tanzania (Die Pflanzenwelt Afrikas - Teil B. Berlin, 1895, 357).

- Braun tells the Masai (Tanzania) use it for wood-carving (Neil Gew. Pfl. Bd. XI, 2, 47).

10 - Thonner is generally speaking about the plant precious medicinal properties using its leaves in fumigations and infusions (Die Blutenpflanzen Afrikas - Berlin 1908).

- Dragerdorff tells that this species have the same therapeutic applications as *Salvia officinalis* (sage) (Die Heilpflanzen - Stuttgart 1898, 589).

15 - Canzonieri and Spica made some studies about the supposed antipyretic properties/activities of *Tarchonantus Camphoratus* leaves (Gazz. Chim. Ital. 1882, 227).

- Watt and Breyer tell the Ottentotti and other indigenous in the South Africa smoke the plant leaves using it as tobacco thanks to their slight narcosis forms. They are also used in fumigations against headache, rheumatism and infusions (The medicinal and poisonous Plants of South Africa - Edimburg - 1932, 189) against dyspepsia and toothache.- Pappe tells leaves contain some camphor but he gives no practical proof (Florae Capensis Medicinae Prodromus - Capetown - 1868, 178).

20 - Pijper distilled an essential oil but he gave no

details on its characteristics (De Volksgeneskunst in Transvaal - Leyden, 1919).

- De Stefanis distilled, using some small branches with leaves sent from Eritrea to the Farmacognosia Laboratory of Turin University, an essence having a strong camphorated smell, with a yield of 0.1% and the following peculiarity:
5 D 0,9152; i.a. 2,1; i.s. 11,8; i.s. after acetylene 85; I. Iodine 188,5; solubility 1:0,5
in alcohol at 95° (Boll. Inf. Econ. Minist. Colonie - Roma, 1924, n. 1).
- Further details come from Rovesti's documentation which shows two plant distillations made in February (dried season) and in August (damp season) which took place in the Ethiopian tableland (XXIX International Congress of
10 Industrial Chemistry, above cited).
15

	Yield%	d ₁₅ [°]	d ₂₀ [°]	n _D ²⁰	I.S. after acethyl.	I.S. sol.
February essence	0.108	0.9171	-7°23'	1.4681	31.73	149.33 1:3A 70°
August essence	0.209	0.8968	-2°15'	1.4718	18.67	41.07 1:3A 90°

It has now been found, and this is the subject of this invention, that some parts of the plant, in particular its leaves, fresh or dried and their derivatives, have some special insect repelling, 5 insecticide, anti-oedema, decongestant, anti-irritating and smoothing properties that might be profitably used for therapeutic applications both for humans and animals.

10 The derivatives of this invention concern the Tarchonanthus camphoratus extracts obtained through an extraction as mentioned for example in the Italian Pharmacopeia.

15 Few examples of extraction methods are: maceration, decoction, percolation and distillation.

There are then different derivatives such as the aqueous, the glycolic, the alcoholic, the hydroalcoholic, the soft and dried ones and, preferably, the essential oils.

20 One of the main goals of this invention is the use of the essential oil. According to the present invention, the application of this plant and of their derivatives concerns not only its insect repelling and insecticide action but also the treatment of irritations and inflammations caused by insect bites.

25 The efficacy of the Tarchonanthus camphoratus derivatives has been also found during some irritation and inflammatory conditions on cutis as for example eczema, acne, reddening, swelling and on genital and mouth mucosa.

30 The Tarchonanthus Camphoratus essential oil obtained through a distillation in a steam flow, has

been characterized using a GC/MS analysis, in this way 44 components were identified. Among these elements we find:

	Alpha Pinene	15.40%
5	Camphene	4.35%
	Beta Pinene	3.50%
	Delta-2-Carene	4.30%
	Alpha Phellandrene	1.60%
	Limonene	3.00%
10	Gamma Terpinene	2.05%
	Terpinolene	1.35%
	1,8 Cineole	12.10%
	Fenchol	14.40%
	1-Terpinen-4-ol	2.30%
15	Alpha Terpineol	4.50%
	Fenchone	0.85%
	Trans Caryiophyllene	1.15%
	Bergamotene	4.50%
	Delta Cadinene	1.40%
20	Alpha Curcumene	1.70%

The results of this research were presented at the Digne Congress in September 1992 (Ghizzoni, Rovesti, Colombo, Bottini).

Basing on a test of primary cutis irritation on 25 human, it appears that the Tarchonanthus camphoratus oil spreaded as it is on 20 volunteers' healthy cutis in occlusive conditions, gave a medium irritation index of 0.4 after 15 minutes and of 0.35 after 24 hours the sample removal. Basing on the above mentioned parameter 30 the product is then classified as non irritating.

The essential oil showed some surprising

therapeutic anti-oedema properties. The information about the applications of the essential oil, concerns in detail the oedema status on lower limbs.

Another object of the present invention are the 5 topical pharmaceutical compositions containing from 0.01 to 10% of Tarchonanthus camphoratus essential oil used as an active ingredient, alone or combined with other active materials.

The compositions can be made according to 10 conventional methods as reported, for example, in the "Remington's Pharmaceutical Sciences Handbook" Mack Pub. N.Y. U.S.A.

Some examples of pharmaceutical topical compositions are: solutions, suspensions, emulsions, 15 ointments, creams, toothpastes in gel form, sprays, prolonged release compositions such as transdermic plasters, and soaps.

One of the preferred embodiments of this invention is the preparation of insect-repelling and insecticide 20 formulations containing from 0.01 to 10% of Tarchonanthus camphoratus essential oil as active ingredient, alone or with other similar components having the same activity.

Some examples of these preparations are: mosquito-fumigants, fumigants, vaporizing solutions, plates, 25 sprays, stick, lotions, creams and gels.

The Tarchonanthus essential oil, put in different topical compositions having anti-oedema, decongestant, anti-irritating, soothing activity, can be used in 30 quantities ranging from 0.01% to 5%, preferably from 0.03% to 0.5%.

On the other side the Tarchonanthus essential oil, put in different topical formulations with insect-repelling and insecticide activity, can be used in quantities ranging from 0.03% to 7%, preferably from 5 0.05% to 3%.

In insect-repelling formulations, where the shrub or its essential oil are used at their natural state, the quantity must be 5% up to 95%. In this case it is advisable to use the plant during its balsamic period 10 and immediately after its picking up; this, unfortunately, sets a limit to the Tharconanthus use at natural state, while no limit is fixed for its essential oil.

The activity of the essential oil, being part of 15 this invention, has been tested in more than one pharmacological and clinical test.

1. Insect-repelling and insecticide activity.

A spray lotion containing 0.05% Tarchonanthus essential oil, in respect to the below mentioned 20 formulation in example n. 1, was spreaded on 10 volunteers' skin who, during summer season evenings, laied in places with a high mosquitoes concentration.

It has been showed that among the 10 volounteers only 2 of them had mosquito-bites on two cutis areas.

25 A spray lotion containing 3% Tarchonantus essential oil, in respect to the below mentioned formulation in example n. 3, was spreaded on 10 volunteers' skin who laied in places with a high mosquitoes concentration during summer evenings. It was 30 showed that none of them had bites on the skin.

A Tarchonanthus camphoratus essential oil alcoholic

lotion, in respect to the below mentioned formulation in example n. 4, was used in a diffusor with absorbant tampon and put in a dimly airy room of about 60 mc infested with bothersome insects. Once the diffuser 5 worked, an insecticide action started.

2. Anti-oedema, decongestant, anti-irritating and soothing activity.

An application of 0.1% Tarchonanthus essential oil gel, as per formulation in example 5, was spreaded on 10 oedematous legs, which gave immediate relief.

A gel containing 0.05% Tarchonatus essential oil, as per formulation in example 6, was put on female genitals with itching problems. That brought an immediate relief.

15 A gel containing 0.05% Tarchonanthus essential oil was used as per formulation in example 5, against bags under one's eyes. A rapid and surprising recovery took place.

20 A gel on 0.3% Tarchonantus essential oil basis, as mentioned in example n. 9, was used on a right ear as a remedy for a swelling due to a mosquito, or some other unidentified insect-bite. The problem was immediately solved. The same result was obtained after an application on different skin areas on 10 persons with 25 various insect bites.

25 A gel on 0.05% Tarchonantus essential oil basis, as mentioned in example n. 6, was spreaded on 10 persons suffering from frequent erythema generally treated with a cortisone cream. It was found that all 30 the subject recovered rapidly and both the painful and itching sensations disappeared.

An alcoholic solution containing 0.1% Tarchonanthus essential oil, see example n. 12, was put, by means of a tampon, on a pimply skin full with acne on 10 patients. In all the above mentioned situations the 5 problem was totally solved. The same preparation was put on recent pimples that disappeared 24 hours later.

A gel with 0.1% Tarconanthus essential oil was used, as per example n. 7, on 5 subjects' face and neck skin and on armpits and legs suffering from irritation 10 after shaving and depilation treatments. They both declared a relief and freshness sensation.

A fluid emulsion containing 0.1% Tarchonanthus essential oil, as per example n.13, was spreaded on genital and anal areas on 2 aged people and on 3 new 15 borns, suffering from itching conditions due to napkins use. All the cases were solved rapidly.

A fluid emulsion on 0.1% Tarchonanthus essential oil, see example 14, was spreaded on bedsores on 3 patients. In all these cases the recovery was rapid, 20 the oedema and the irritation improved.

A gel containing 0.5% Tarchonanthus essential oil, as per example n. 6, was spreaded on 7 subject with 25 itching problems on the anal area due to emorrhoids and rhagades. They recovered rapidly declaring a freshness and relief sensation.

A mouthwash with 20% infusion, worked at cold state, obtained from Tarchonanthus grinded fresh leaves, as in example n.16, was used on 5 patients having 30 irritated gums. In these cases a constant and periodic application brought a relief with a consequent decongestion of gums together with a freshness

sensation and a good smelling breath.

A toothpaste with 0.2% Tarchonanthus essential oil, as mentioned in example n. 15, was used in 5 cases suffering from slightly irritated gums. A constant and 5 periodic use of the formulation was of help in the gums decongestion. A freshness sensation and a good smelling breath was also noticed.

An alcoholic gel containing 1% Tarchonanthus essential oil, as per example n. 10, was used on legs 10 suffering from phlebitis. A constant and periodic use was of help to solve the problem.

An alcoholic gel containing 0.8% Tarchonanthus essential oil as per example n. 11, was spreaded on haematoma on 3 subjects. In both cases, a constant and 15 periodic use, was of help to improve the oedema problem.

The following examples further illustrate the invention. For sake of brevity, the essential oil is called E.O.

20 **EXAMPLE N. 1**

Insecticide spray lotion

PEG 40 Hydrogenated Castor Oil	0.2	%
Glycerine	3	%
Tarchonanthus camphoratus E.O.	0.05	%
25 Preservatives (antibacterial/antimould)	q.s.	
Demineralized water	q.s.	to 100%

EXAMPLE N. 2

Insecticide spray lotion

PEG 40 Hydrogenated Castor oil	4	%
30 Glycerine	3	%
Tarchonanthus camphoratus E.O.	1	%

	Preservatives (antibacterial/antimould)	q.s.
	Demineralized water	q.s. to 100%

EXAMPLE N. 3Insecticide spray lotion

5	Peg 40 Hydrogenated Castor Oil	12	%
	Glycerine	3	%
	Tarchonanthus camphoratus E.O.	3	%
	Preservatives (antibacterial/antimould)	q.s.	
	Demineralized water	q.s. to 100%	

10 EXAMPLE N. 4Insecticide alcoholic solutions for environmental purposes

	Methylated alcohol type A	42	%
	Tarchonanthus camphoratus E.O.	5	%
15	Sorbitan monoleate 20 (OE)	13	%
	Demineralized water	q.s. to 100%	

EXAMPLE N. 5Ante-oedema gel

	Carboxyvinyl polymer (Carbomer 940)	0.76	%
20	Glycerine	3	%
	Sorbitan 20 (OE) monolaurate	0.4	%
	Tarchonanthus camphoratus E.O.	0.1	%
	Preservatives (antibacterial/antimould)	q.s.	
	Triethanolamine	0.5	%
25	Demineralized water	q.s. to 100%	

EXAMPLE N. 6Anti-irritating, soothing gel

	Carboxyvinyl polymer (Carbomer 940)	0.76	%
	Glycerine	3	%
30	Sorbitan 20 (OE) monolaurate	0.2	%
	Tarchonanthus camphoratus E.O.	0.05	%

	Preservatives (antibacterial/antimould)	q.s.
	Triethanolamine	0.5 %
	Demineralized water	q.s. to 100%

EXAMPLE N. 7**5 Anti-irritating gel pre/after shave/depilation**

	Carboxyvinyl polymer (Carbomer 940)	0.5 %
	Glycerine	3 %
	Sorbitan 20 (E.O.) monolaurate	0.2 %
	Tarchonanthus camphoratus E.O.	0.04 %

10	Preservatives (antibacterial/antimould)	q.s.
	Triethanolamine	0.3 %
	Demineralized water	q.s. to 100%

EXAMPLE N. 8**After sun gel**

15	Carboxyvinyl polymer (Carbomer 940)	0.76 %
	Glycerine	3 %
	Sorbitan 20 (OE) monolaurate	0.4 %
	Tarchonanthus camphoratus E.O.	0.1 %
	Preservatives (antibacterial/antimould)	q.s.
20	Triethanolamine	0.5 %
	Demineralized water	q.s. to 100%

EXAMPLE N. 9**Anti-oedema gel**

	Carboxyvinyl Polymer (Carbomer 940)	0.70 %
25	Glycerine	3 %
	Sorbitan 20 (OE) monolaurate	1.2 %
	Tarchonanthus camphoratus E.O.	0.3 %
	Preservatives (antibacterial/antimould)	q.s.
	Triethanolamine	0.45 %
30	Demineralized water	q.s. to 100%

EXAMPLE N. 10Anti-oedema alcoholic gel

	Carboxyvinyl polymer (Carbomer 940)	0.5	%
	Alcohol type D	40	%
5	Glycerine	5	%
	Peg 40 Hydrogenated Castor Oil	3	%
	Tarchonanthus camphoratus E.O.	1	%
	Preservatives (antibacterial/antimould)	q.s.	
	Triethanolamine	0.3	%
10	Demineralized water	q.s. to 100%	

EXAMPLE N. 11Soothing/refreshing alcoholic gel

	Carboxyvinyl polymer (Carbomer 940)	0.5	%
	Alcohol type D	40	%
15	Glycerine	5	%
	Peg 40 Hydrogenated Castor Oil	2.5	%
	Tarchonanthus camphoratus E.O.	0.8	%
	Preservatives (antibacterial/antimould)	q.s.	
	Triethanolamine	0.3	%
20	Demineralized water	q.s. to 100%	

EXAMPLE N. 12Alcoholic solution for pimply skins

	Alcohol type C	40	%
	Glycerine	2	%
25	Sorbitan 20 (OE) monolaurate	2	%
	Tarchonanthus camphoratus E.O.	0.1	%
	Lavender e.o.	0.4	%
	Demineralized water	q.s. to 100%	

EXAMPLE N. 13Anti-irritating fluid emulsion

	Carboxyvinyl polymer (Carbomer 940)	0.30	%
	Glycerine	6	%
5	Tarchonanthus camphoratus E.O.	0.1	%
	Triethanolamine	0.2	%
	Acethylated Lanoline	1	%
	Dimethylpolyxyloxane	1	%
	Myristil lactate	2	%
10	Decyle oleate	2	%
	Preservatives (antibacterial/antimould)	q.s.	
	Demineralized water	q.s.	to 100%

EXAMPLE N. 14Anti-irritating/decongestant fluid emulsion

15	Carboxyvinyl polymer (Carbomer 940)	0.30	%
	Glycerine	6	%
	Tarchonanthus camphoratus E.O.	0.1	%
	Allantoine	1	%
	Tocopheryl acetate	0.5	%
20	Triethanolamine	0.2	%
	Acethylated lanoline	1	%
	Dimethylpolyxiloxane	1	%
	Myristil lactate	2	%
	Decyl oleate	2	%
25	Preservatives (antibacterial/antimould)	q.s.	
	Demineralized water	q.s.	to 100%

EXAMPLE N. 15Gum toothpaste

	Potassium sorbate	0.2	%
30	Glycerine	11	%
	Sorbitan 20 (OE) monolaurate	0.8	%

	Tarchonanthus camphoratus E.O.	0.2	%
	Carboxyvinyl cellulose medium density	1.5	%
	Dicalcium phosphate di-hydrate	48	%
	Sorbitol 70%	11	%
5	Sodium laurilether sulphate	2	%
	Acesulfame Hoechst (sweetener)	0.2	%
	Preservatives (antibacterial/antimould)	q.s.	
	Demineralized water	q.s. to 100%	

EXAMPLE N. 16

10	<u>Idroalcoholic mouthwash</u>		
	Alcohol type E	15	%
	Glycerine	4	%
	Glycyrrhizinate ammonium	0.1	%
15	Tarchonanthus infusion at cold state grinded fresh leaves at slow stirring for 7 days in demin. water preserved	20	%
	Demineralized water	q.s. to 100%	

EXAMPLE N. 17

	<u>Mosquito fumigant</u>		
20	A convenient quantity of dried leaves, belonging to a plant picked up by no more than 30 days, was grinded small.		
	30% of it was mixed up with arabic gum (10%), pit-coal (50%) potassium nitrate (10%), worked in water, spiral shaped and dried in a heater at 35°C for 24 hrs.		
25			

The same examples can be formulated with extracts and soaked in the proper concentrations.

CLAIMS

1. The use of *Tarchonanthus camphoratus* parts or a derivative thereof as insect-repelling, anti-irritating, soothing, anti-oedema, or decongesting agent.
- 5 2. The use of *Tarchonanthus camphoratus* extracts as an insect-repelling, anti-irritating, soothing, anti-oedema, or decongesting agent.
- 10 3. The use of *Tarchonanthus camphoratus* essential oil as insect-repelling, anti-irritating, soothing, anti-oedema, or decongesting agent.
4. A topical pharmaceutical composition containing *Tarchonanthus camphoratus* as active ingredient.
- 15 5. A topical pharmaceutical composition containing *Tarchonanthus camphoratus* parts, derivative, extract or essential oil as active ingredient in a concentration of 0.05 to 10%.
6. The use of *Tarchonanthus camphoratus* parts, or a derivative thereof in the preparation of an insect-repelling or insecticide formulation.
- 20 7. The use of *Tarchonanthus camphoratus* extract in the preparation of an insect-repelling or insecticide formulation.
- 25 8. The use of *Tarchonanthus camphoratus* essential oil in the preparation of an insect-repelling or insecticide formulation.
9. An insect-repelling or insecticide formulation containing 5% to 95% of *Tarchonanthus camphoratus* parts, derivative, extract or essential oil.
- 30

INTERNATIONAL SEARCH REPORT

Internal Application No

PCT/EP 93/02997

A. CLASSIFICATION OF SUBJECT MATTER

A 01 N 65/00, A 61 K 35/78, A 61 K 7/16

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

A 01 N, A 61 K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	LA GAZZETTA CHIMICA ⁷ ITALIANA, An. XII, vol. XII, 1982, Palermo F. CANZONERI et al. "Ricerche sui Tarchonanthus Canphora- tus", pages 227-31, the whole document. --	1-9
A	CHEMICAL ABSTRACTS, vol. 91, no. 25, issued 17 October 1979 (Columbus, Ohio, USA), F. BOHLMAN et al. "Naturally occurring terpene derivati- ves. Part 189. A new bisab- olene derivative and a new dihydrocafeic acid deriva- tive from Tarchonanthus trilobus."	1-9

 Further documents are listed in continuation of box C. Patent family members are listed in annex.

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INTERNATIONAL SEARCH REPORT

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Internat.	Application No
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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>page 704, abstract no. 211594p & Phytochemistry 1979, 18(4), 677-8. --</p> <p>DERWENT ACCESSION No. 66-33 730, Questel Telesystems (WPIL), DERWENT PUBLICATIONS LTD., London, abstract & ZA 6704243 (WILMANS JJ). ----</p>	1-9

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